

# Study of the pattern of improvement in androgenetic alopecia in patients using microneedling associated with minoxidil and/or platelet-rich plasma and mesotherapy

Estudo do padrão de melhora da alopecia androgenética em pacientes com uso de microagulhamento associado a minoxidil e/ou plasma rico em plaquetas e mesoterapia

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## Abstract

**Introduction:** alopecia linked to androgenic hormonal factors is something that has long been the subject of studies and knowledge applications worldwide. This pattern of hair loss, mainly related to males, has therapies that are currently limited to interruption of hair loss with slight growth progression in some cases. In this regard, a new microneedling technique, with or without adjuvant therapies, associated with well-established methods such as minoxidil has led the treatment of this esthetic alteration to better levels of results. **Objective:** to conduct an investigation into the current results of research involving microneedling associated with the use of Minoxidil, platelet-rich plasma and/or mesotherapy. **Methodology:** searches were conducted in the PubMed and Scielo database in April 2021, searching for the terms “minoxidil AND microneedling”. **Results and Discussions:** the results obtained have converged to the proposal that the association of the rolling method (microneedling) with the topical application of a vasodilator (minoxidil) presents a pattern of hair growth never achieved by the available conventional therapy, and that, if added platelet-rich plasma and/or solutions through mesotherapy, the results can be even more advantageous. **Conclusion:** further studies are needed to cover aspects that have not yet been elucidated for the treatment of alopecia, however, the results obtained so far are promising for the success of hair replacement.

**Keywords:** Microneedling, Minoxidil, Alopecia

## Resumo

**Introdução:** a alopecia ligada a fatores hormonais androgênicos é algo que há muito tempo tem sido alvo de estudos e aplicações de conhecimento científico em todo mundo. Este padrão de perda capilar, principalmente ligada ao sexo masculino dispõe de terapias que atualmente se limitam à interrupção da queda de fios com leve progressão de crescimento em alguns casos. Neste tocante, uma nova técnica de microagulhamento, com ou sem terapias adjuvantes, associado a métodos já consagradas como minoxidil tem levado o tratamento desta alteração estética para melhores níveis de resultado. **Objetivo:** conduzir uma investigação sobre os resultados atuais de pesquisas que envolvam o microagulhamento associado ao uso de Minoxidil, plasma rico em plaquetas e/ou mesoterapia. **Metodologia:** foram feitas pesquisas no banco de dados da PubMed e Scielo em abril de 2021 buscando-se os termos “minoxidil AND microneedling”. **Resultados e Discussões:** os resultados obtidos têm convergido para a proposta de que a associação do método de rolagem (microagulhamento) com a aplicação tópica do vasodilatador (minoxidil) apresenta um padrão de crescimento capilar nunca alcançado pela terapia convencional disponível, e que, se acrescentar plasma rico em plaquetas e/ou soluções através da mesoterapia, os resultados podem ser ainda mais vantajosos. **Conclusão:** novos estudos são necessários para abranger as vertentes ainda não elucidadas para o tratamento da alopecia, contudo, os resultados até aqui obtidos são promissores para o sucesso da reposição capilar.

**Palavras chave:** Microagulhamento, Minoxidil, Alopecia

## Introduction

Androgenetic alopecia (AGA) is a chronic dermatological condition in which capillaries loss occur. Despite following men and women, it is more prevalent in males, given its close relationship with the hormones that give name to this pattern of fall(1) and which are

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less present in females. Currently, treatments consist of local therapies, oral and surgical procedures. The most used drugs are minoxidil in its topical form and oral finasteride(2-5).

AGA is caused by a combination of genetic factors and androgen hormones. In women, it can also be caused by endocrinopathies associated with an increase in these same hormones(2,6). Currently, among ethnic groups, the caucasian is the one with the highest incidence of the disease. About 80% of caucasian men aged around 70 years have the alteration, whereas in caucasian women of the same age the prevalence can reach 42%(3). Although a high prevalence can be observed in the elderly, the disease can affect individuals at puberty(3,7).

Current treatments are aimed at controlling alopecia, helping to stabilize and recover part of the hairs, but there is still no complete repilation after the treatment(8, 1). Drug therapies such as finasteride or dutasteride act by preventing the metabolism of testosterone into dihydrotestosterone(3,9-10). Minoxidil widely used topically and more recently orally has an important and recognized action in the treatment of this condition(9-12). Recently, the different mechanisms by which it acts against AGA have been clarified: stimulating vasodilation that increases local growth factors, activating cytoprotective prostaglandins, decreasing perifollicular inflammation, inducing the Wnt/ $\beta$ -catenin signaling pathway, which has effects on the synthesis of DNA and cell proliferation, in addition to a possible anti-androgenic interaction, influencing both the telogen and anagen phase of the strands(3-4).

Other therapies for capillary stimulation have been shown in the literature, such as vitamins and amino acids, or photobiomodulation(4). Among these, a therapy has emerged as an important part in the treatment against AGA, the microneedling. This intervention is performed through skin microperforations in which the technique is performed using surgical steel micro-needles, ranging between 0.5 and 2.5 mm in length, which, through a cylindrical bearing, slides over the skin in the stratum corneum(13-14). The length of the needle as well as the number of times the epidermis will receive the perforations can impact the success of the treatment. In this regard, studies are being carried out to establish a standard protocol for this technique(15-16). The interval between microneedling applications in the work methodology varies between 1 to 2 weeks.

It is believed that microneedling enhances the effect of drugs used for AGA, acting on the formation of new blood vessels (angiogenesis), stimulating platelet-derived growth incentives and cell regeneration, as well as increasing collagen and elastin(5,17). Studies have shown that microneedling facilitates

transdermal permeation by inducing the transport of chemically active substances through superficial skin levels. This way, it increases the drug concentration, making it more effective (5,17-18).

The microneedling technique in conjunction with other drugs for AGA has aroused interest due to the possibility of generating better results than the treatments currently recommended, as it presents a relatively low value and is easy to perform(16,19-20). In view of the promising results of this treatment, and due to its incipience, this research aimed to evaluate the available knowledge about the effectiveness of this procedure, seeking the results obtained with the microneedling technique associated with the use of topical minoxidil and the application of mesotherapy or rich plasma in platelets (PRP), compared to traditional methods in the literature (topical minoxidil and oral finasteride) for the treatment of AGA. Thus, it is expected to link existing knowledge and guide questions for future research.

## Methodology

### Methodological Strategy

In order to expose a quality marker for this research, we sought to obtain the results by the PRISMA recommendation (Preferred report items for systematic reviews and meta-analyses) for systematic reviews(21).

Regarding the clinical importance of this approach, we used the PICO strategy (Patient, Intervention, Control, Result)(22) and the order in which the questions in this acronym are answered are:

- Patients: those who suffered hair loss due to AGA;
- Intervention: mechanical / chemical treatment for AGA;
- Control: comparison of patients who received application of this technique and transaction with topical 5% minoxidil;
- Outcome: post-therapy evaluation of the standard and control groups.

### Search criteria

Scientific database tools were used to research new techniques for patients with alopecia. The bibliographic databases selected for this review were PubMed (US National Library of Medicine and Institutes of Health) and Scielo (Scientific Electronic Library Online).

Aware of the need for a common language for database searches, we used the DeCS (Health Science Descriptor) and MeSH (Medical Subject Headings) indexing and retrieval of subjects in the literature. The main words of this work and that were applied in the

searches were “minoxidil” and “microneedling” or “microagulhamento” for searches in the descriptor of the BVS (Virtual Health Library). The descriptor presented after the search was just “minoxidil” for the MeSH and DeCS search. The absence of descriptors involving agulha (in Portuguese or microneedling in English) is probably due to the fact that this technique has recently been incorporated into clinical treatments. All searches were performed in April 2021, with no limitation on publication date or other site database filters. To join the descriptors, the Boolean operator “AND” was used.

### Eligibility Criteria

In the analysis of the works, the three authors evaluated the results shown by the searches. The first two jointly evaluated the results, while a third author re-evaluated this initial filtering. For this, a title + abstract evaluation was initially carried out. After these two items are consistent with the research, the methodology of the article was observed.

As for the methodological standard of the scientific article, preference was given to prospective, case-control, randomized and/or double-blind studies of patients who suffered hair loss due to androgenic alopecia and who were primarily submitted to microneedling analysis by dermaroller with minoxidil, with or without plasma rich in platelets (PRP) and/or drug injections (mesotherapy), and their results in stimulating follicles in the scalp.

In this search, the Scielo database did not generate any outcome for the research, both the terms in

English and Portuguese, probably due to the recent nature of this line of study. In PubMed, 30 papers were presented by searching for the terms “minoxidil AND microneedling”, some of which were in the standard literature reviews and other formats that did not converge with our searches, such as microneedling by other techniques (electrodynamics, radiofrequency), made in mice or other differences, making it necessary to individually analyze the articles to homogenize the study, select and incorporate it into this review.

### Results

In order to enhance the work, in addition to the main promoter axis (isolated minoxidil or associated with microlesions by needling), publications were chosen that also implemented other methods, such as the addition of platelet-rich plasma or topical mesosolution (aggregate of vitamins, amino acids, minerals and other components).

After individual analysis of the 30 results obtained by PubMed, 9 studies remained that matched the same line of scientific clarification proposed for this topic, according to the algorithm below (Figure 1).

In the tables below, an aggregation of the analysis of the authors in their respective works is built, which are in line with a demonstrative line of this new therapy for AGA.

In the second table, we compile the studies that associate the mechanical effect of microneedling with the effect of platelet-rich plasma or topical mesosolution (Table 2). This mesosolution generally consists

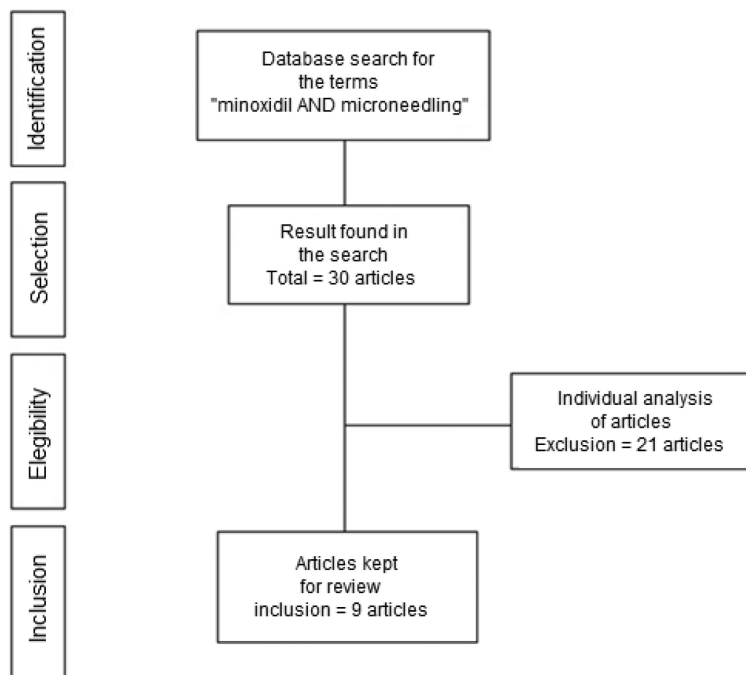


Figure 1 - Search and selection algorithm for articles in a database.

Table 1

**Studies that assess improvement in the association of microneedling against the isolated use of minoxidil.**

<i>Author</i>	<i>Methodology</i>	<i>Results</i>
Kumar et al. <sup>(23)</sup>	- Sample: 68 patients (male) - Research time: 12 weeks - Methodology: patients with grade III and IV androgenic alopecia were divided into two groups, the first with weekly microneedling + application twice a day of minoxidil 5%, while the second only received the application of medication at the same frequency.	The group that received combination therapy had an average increase in hair count of 12.52/inch <sup>2</sup> , while the second group had only 1.89/inch <sup>2</sup> . The second test applied was the self-assessment, and in the first group, 4 patients reported an improvement of 50% compared to none in the second group.
Dhurat et al. <sup>(24)</sup>	- Sample: 4 patients (male) - Research time: 6 months of microneedling and 18 months after the procedure. - Methodology: Patients who were already using finasteride + minoxidil 5% but with no improvement in their capillary growth were submitted to weekly needling of the scalp.	Patients were followed for 18 months after therapy to assess sustainability of response. On the 7- points scale assessment, all patients showed a +2 or +3 result. Therefore, the author concluded that the response was satisfactory with the addition of needling for patients refractory to conventional treatment and that this response was maintained over the months following therapy.
Dhurat et al. <sup>(25)</sup>	- Sample: 100 patients (male) - Research time: 12 weeks - Methodology: comparative study, blind, for 12 weeks. 50 patients received a weekly session of microneedling + 5% minoxidil 2x/day while the second group received only the topical solution.	The hair count evaluation showed a constant increase in the linear pattern over the weeks, with the slope of the curve with dermaroller being greater than that of the control group (91.4 vs 22.2). 40 patients in the microneedling group had a +2 to +3 response on the 7 point scale versus none with the same improvement as in the minoxidil group.
Faghihi et al. <sup>(26)</sup>	- Sample: 60 patients (male and female) - Research time: 12 weeks - Methodology: this study seeks to elucidate whether there is improvement in alopecia with the use of minoxidil associated with biweekly microneedling and whether the best results are obtained with 0.6 or 1.2 mm of skin depth	Microneedling with a depth of 0.6mm associated with minoxidil in terms of both hair count and hair thickness was observed to tend to be more beneficial than 1.2mm of integumentary perforation.
Fujita <sup>(27)</sup>	- Sample: 1 patient (male) - Research time: 14 weeks - Methodology: the use of minoxidil twice a day on the right scalp was used in this patient, while on the left side minoxidil was associated with weekly microneedling	On the side where there was the combined therapy, the study reports that the hair density by the trichoscope was significantly increased compared to the monotherapy side
Sohng et al. <sup>(28)</sup>	- Sample: 29 patients (male and female) - Research time: 6 months - Methodology: they were divided into 3 groups for the use of procedures at home: group 1 only minoxidil; second group use of minoxidil and microneedling; third group only microneedling	At month 6 an improvement in the results was observed in the composite treatment group, but the observed differences did not reach statistical significance between the groups. The patient's self-assessment followed the same trend, however, the work still concludes that microneedling for domestic use can be a therapeutic modality.

of vitamins, amino acids, coenzymes, mining and/or nucleic acids<sup>29</sup>.

**Evaluation of results**

Therapy based on the use of topical minoxidil and oral finasteride acts to reduce hair loss, with a small increase in the number of hairs, but mainly acting on thickening their thickness<sup>(24,32-33)</sup>, the cosmetic effect being isolated of minoxidil less significant. These points are shown as one of the causes of the patient's current abandonment of conventional therapy<sup>(34)</sup>.

The new microneedling therapies, in addition to the experimental demonstration of their good results,

have the following theoretical support to outline their functionality<sup>(25,35-36)</sup>.

- Release of growth factors during the regeneration of skin wounds;
- Activation of stem cells also in the condition of wound healing;
- overexpression of hair growth-related genes such as vascular growth factor, catenin B, Wnt3a and Wnt10b (documented in animal studies).

Generally speaking, the studies have been based on microneedling methodologies with a 1.5mm dermaroller, with frequency of weekly sessions, with 8 rotations per scalp region. As for minoxidil, its concentration is generally 5%, with two daily applications.

Table 2

**Studies that correlate the test group (microneedling + minoxidil with or without PRP and mesotherapy) with the control group (minoxidil).**

<i>Author</i>	<i>Methodology</i>	<i>Results</i>
Gajjar et al <sup>(29)</sup>	- Sample: 49 patients (male) - Research time: 16 weeks - Methodology: for 4 months, the population was divided into two groups: the first group received intralesional mesosolution with microneedling in 8 sessions (group A), the second group received only 5% minoxidil twice a day (group B).	The result shows an increase in the hair shaft when comparing the pre and post treatment of group A with group B. The observation concluded by the author, however, emphasizes that there is no difference between mesotherapy and minoxidil.
Jha et al <sup>(30)</sup>	- Sample: 93 patients (male) - Research time: 12 weeks - Methodology: patients were divided into 3 groups: A – minoxidil 5% twice a day; B – minoxidil 5% + PRP (at 3-week intervals); C- 5% minoxidil + PRP (3 week intervals) + microneedling (1.5 mm)	The work shows a synergism between platelet-rich plasma and minoxidil. He claims that their association demonstrates superior results to the isolated use of these two compounds.
Shah et al <sup>(31)</sup>	- Sample: 50 patients (male) - Research time: 6 months - Methodology: patients were divided into two groups, where the first received only 5% minoxidil application, while the second group received 5% minoxidil + microneedling + PRP.	Patients in the second group reported an improvement, both in a moderate and excellent pattern, when compared to the first group.

The results of the application of microneedling associated with the previously described use of minoxidil and/or PRP and mesosolution seem to generate effects previously unattainable with traditional treatment. All papers that were evaluated by this review showed capillary improvement with an increase, to some degree, in the number and/or thickness of strands with minimal side effects. In general, the studies used a 7-point scale (Table 3), phototrichogram, triscope and/or patient self-assessment as growth assessment.

Table 3

**Scale of 7 points of improvement rating.**

<i>Classification</i>	<i>Rating score</i>
Severe worsening	-3
Moderate worsening	-2
Mild worsening	-1
No change	0
Mild improvement	+1
Moderate improvement	+2
Excellent improvement	+3

A point that should be emphasized in this theme is that, although the results achieved so far are positive, there are still few publications and samples found in the literature(37).

Another point to be highlighted are the side effects

shown in the studies. As new actions are of great value, with optimal results achieved by a relatively simple therapy, side effects are reasonably rare and small, such as local pain, erythema, headache, bleeding, seborrheic dermatitis and rarely scars(31,38-39).

Although this review has as its main point the analysis of the follicular stimulus after microlesions, it is also necessary to incorporate the adjuvant methods to this one that are being studied, such as the application of PRP, which alone already showed a beneficial result(33-34), and when added with needling, it has even better effects(31).

In addition to the point described above, it was also seen that in the temporal issue, over the weeks of the study, therapy with dermaroller associated with minoxidil was statistically superior to the control group of isolated use of the topical application of the solution, being sustained even after months of research.

**Conclusion**

Modern techniques, such as microneedling, have shown promising results for the treatment of AGA, however, their efficiency still needs to be tested and supported by scientific evidence, both in terms of sampling and in the long term. The current methodology has become strengthened and replicated, however, there is still no complete mapping of what is the best needle size or frequency of sessions for the treatment, with a lack of further studies in human beings regar-

ding the different techniques used and confirmation the success rate that these can present.

Based on the results shown so far, this seems to be a favorable future in the minimization of AGA, a problem of a society that has increasingly invested in aesthetic results.

In addition, it is worth highlighting the need for researchers to also describe in more detail the possible adverse effects of the use of microneedling for alopecia, obtained through the increase in the sample quantity and longer post-procedure evaluation time.

In short, microlesions seem to elevate results not previously achieved by conventional techniques, being a promise for future patients who will undergo such a procedure, however, the conclusions of research with microneedling still need to be expanded to delineate and optimize the management of these procedures in order to reduce risks and achieve results that are closer to expectations.

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